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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,718	05/31/2006	Dequan Zhu	ARE-101	5262

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GLOBAL IP SERVICES
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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
06/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,718	ZHU ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/05/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner acknowledges receipt of response to restriction requirement and remarks and amendment filed 04/01/2010. Claims 1-3, 5, 6 and 10 are amended. Claims 7-9 are canceled. Claims 1-6, 10 and 11 are pending.

2. The examiner also acknowledges receipt of IDS filed 05/05/2006

Election/Restrictions

3. Applicant's election with traverse of Group I in the reply filed on 04/01/2010 is acknowledged. The traversal is on the ground(s) that the reference cited to break unity does not mention any molecules from the extract of boxwood and hydrophilic polymer such as polyethylene glycol. This is not found persuasive because Brown in the article Buxus Alkaloids discloses extracts from the boxwood or *Buxus sempervirens L.* and reacts this compound having the cyclovirobuxine structure in claim 4 with ethylene glycol (see page 4421, left column, 1st paragraph from the bottom.

The requirement is still deemed proper and is therefore made FINAL.

4. However also, claims 7-9 have been canceled and the claim 1 has been amended to the specific hydrophilic compound, polyethylene glycol.

5. Linking claims are examined with the elected group. Therefore, claims 10 and 11 are examined with claims 1-6. Furthermore, claim 10 has been amended to depend from the elected claims.

Priority

6. The examiner acknowledges this application as a 371 of PCT/CN04/01259 filed 11/05/2004.

Information Disclosure Statement

7. While the examiner notes that this application is a national stage of the PCT application PCT/CN04/01259 filed 11/05/2004, the references listed on the form 1449 are not in the application file. It is respectfully requested that applicant provide the references to make the application file complete and clear.

Claim Objections

8. Claim 10 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, correction is respectfully requested.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-6, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 recites derivatives of the Cyclovirobuxine and the scope and boundaries of the derivatives of the compound is not clear and the specification has not listed any compounds as derivatives of Cyclovirobuxine.

12.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claim 1-3, 5, 6, 10 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Hu et al. (CN 1444944 A) .

15. Hu discloses pharmaceutical preparation comprising cyclovirobuxine D and polyethylene glycol (see the translation of the whole document). The molecular weight of the PEG is 400 (see claim 4) which anticipates the molecular weight range of 300 to 6000 recited in claim 3. Since the polyethylene molecule reacts with the Cyclovirobuxine at the nitrogen and the ether linkages, the linkages formed are inherently ester, ether and urethane groups so that linking groups of claims 1 and 5 are met. Furthermore, the conjugate recited in claim 6 is inherent because the product of the polyethylene glycol and the Cyclovirobuxine would inherently be any of the compounds recited in claim 6. The composition is a pharmaceutical composition and thus contains pharmaceutically acceptable carrier and excipient, for example, the composition contains vegetable oils and the form of the composition is a pill, so that claims 10 and 11 are met.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-6, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khodzhaev et al. ("Bisquaternary derivatives of cyclobuxine-D and their biological activity," in Chemistry of Natural Compounds, Vol. 33, No. 5, 1997, pp 578-580) and Hu et al. (CN 1444941 A) in view of Zalipsky ("Chemistry of polyethylene glycol conjugates with biologically active molecules," in Advanced Drug Delivery Reviews 16, 1995, pp 157-182).

19. Cyclobuxine extracted from the plant *Buxus sempervirens* is known according to Khodzhaev and that this compound whose structure is the same as that claimed in claim 4 (see structure on page 578 of Khodzhaev); it is also known that this compound has myorelaxant, gangliolytic, hypotensive actions (see last full paragraph of page 578).

20. Furthermore, Hu describes pharmaceutical preparation that comprises Cyclovirobuxine and polyethylene glycol, in which the polyethylene glycol has a molecular weight of 400 (meeting claim 3), and pharmaceutical carriers meeting claim 10, and the form of the pharmaceutical preparation in Hu is a pill (meeting claim 11) (see the whole document translation with emphasis on claims 1-7 and the field of the invention).

21. It is also known in the art that polyethylene glycol conjugates with biologically active agents have been used to deliver biologically active agents (see the whole document of Zalipsky).

22. The structure of cyclobuxine as shown on page 578 lends itself conjugation with the polyethylene glycol at the nitrogen and the oxygen so that the linking groups recited in claims 1 and 5 are met and the conjugate product formed from the polyethylene glycol and cyclobuxine would inherently be that claimed in claims 4 and 6. The polyethylene glycol meets claim 2.

23. While Khodzhaev describes the compound from the extract of the plant *Buxus sempervirens*, and while Hu discloses composition comprising the critical compound and polyethylene glycol and pharmaceutically acceptable carrier, the combined teaching of Khodzhaev and Hu do not specifically say that the composition comprising the critical compound of the claims is in conjugation with the polyethylene glycol or combined teaching of Khodzhaev and Hu is silent as to whether the cyclobuxine/ Cyclovirobuxine is conjugated to the polyethylene glycol.

24. But Zalipsky teaches that pharmacological agents are conjugated to polyethylene glycol for effective delivery of the drugs. Therefore, taking the teachings of Hu and Khodzhaev in view of Zalipsky, one having ordinary skill in the art at the time the invention was made would reasonably expect that conjugating the cyclobuxine/ Cyclovirobuxine with the polyethylene glycol as described by Zalipsky would produce cyclobuxine/ Cyclovirobuxine-polyethylene glycol conjugated product that would be more effective delivery vehicle where the PEG often possesses the ability to avoid quick recognition and clearance in vivo (see abstract of Zalipsky).

25. No claim is allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Primary Examiner, Art Unit 1618